Chapter 31

Drugs in Renal Failure

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I. DOSE ADJUSTMENT METHODS

A. Maintenance Dose

In patients with renal insufficiency, the dose may be adjusted using the following methods:

1. **Interval extension (I):** Lengthen intervals between individual doses, keeping dose size normal. For this method, a suggested interval is shown.
2. **Dose reduction (D):** Reduce number of individual doses, keeping interval between doses normal; recommended when relatively constant blood level of drug is desired. For this method, percentage of usual dose is shown. For some medications and indications, specific dosing is provided.
3. **Interval extension and dose reduction (DI):** Both lengthen interval and reduce dose.
4. **Interval extension or dose reduction (D, I):** In some instances, either dose or interval can be changed.

NOTE: These dose adjustment methods do not apply to patients in the neonatal period. For neonatal renal dosing, please consult a neonatal dosage reference (see Chapter 18). Dose modifications given are only approximations and may not be appropriate for all patients or indications. **Each patient must be monitored closely for signs of drug toxicity, and serum levels must be measured when available; drug doses and intervals should be adjusted accordingly.** When in doubt, always consult a nephrologist or pharmacist who has expertise in renal dosing.

B. Dialysis

General recommendations are provided when available. However, factors such as patient age, indication for use, residual native kidney function, specific peritoneal dialysis (PD) or intermittent hemodialysis (IHD) settings, etc., will affect the medication dosing needs of each individual patient. **Consult with a nephrologist or pharmacist who is familiar with medication dosing in dialysis prior to prescribing medications for a dialysis patient.**

II. ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Table 31.1)

TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE[1-5]

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Acyclovir (IV)	Renal (60%–90%)	2–3	Q8 hr	D, I	25–50 10–25 <10/IHD[b]/PD	100% 100% 50%	Q12 hr Q24 hr Q24 hr
Amantadine[c] **Note:** On day 1, give normal dose, then decrease subsequent doses based on renal function.	Renal (80%–90%)	10–30	Q12–24 hr	D, I	30–50 15–29 <15/IHD/PD	50% 50% 100%	Q24 hr Q48 hr Q7 days
Amikacin	Renal (>95%)	1.5–3	Q8–12 hr	I	<60/IHD/PD	Administer a standard one-time dose. Determine the appropriate interval for redosing based on serum concentrations. For IHD, redose based on concentrations.	
Amoxicillin **Note:** Do not administer 875 mg immediate release or 775 mg extended release tablets with eGFR <30 mL/min/1.73 m^2.	Renal (60%)	1–2	Q8–12 hr	D, I	10–30 <10/IHD[b]/PD	50–100% 50–100%	Q12 hr Q24 hr
Amoxicillin/clavulanate **Note:** Do not administer 875 mg immediate release or 1000 mg XR extended release tablet with eGFR <30 mL/min/1.73 m^2.	Renal (60%/25%–40%)	1–2/1	Q8–12 hr	D, I	10–30 <10/IHD[b]/PD	50%–100% 50%–100%	Q12 hr Q24 hr

Amphotericin B	Renal (40%)	Initial: 12–25 Terminal: 15 days	Q24 hr		No guidelines established.		
Amphotericin B lipid complex (Abelcet)	Renal (1%)	Terminal: 7 days	Q24 hr		No guidelines established.		
Amphotericin B, liposomal (AmBisome)	Renal (10%)	Initial: 7–10 Terminal: 4–6 days	Q24 hr		No guidelines established.		
Ampicillin (IV)	Renal (90%)	1–2	Q4–6 hr	I	10–30	100%	Q8 hr
					<10/IHD[d]/PD	100%	Q12 hr
Ampicillin/sulbactam	Renal (90%/ 75%–85%)	1–2/1	Q4–6 hr	I	15–29	100%	Q12 hr
					<15/IHD[d]/PD	100%	Q24 hr
Aztreonam **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function.	Renal (60%–70%) (hepatic)	1-2	Q6–8 hr	DI	10–30	50%–66%	Q8 hr
					<10/IHD/PD	25%–33%	Q12 hr
					IHD: Administer 12% of the full dose as an additional supplemental dose after dialysis in severe infections.[6]		
Cefaclor	Renal (80%)	0.5–1	Q8–12 hr	D	<10/IHD[d]/PD	50%	Q8–12 hr
Cefadroxil	Renal (>90%)	1–2	Q12 hr	I	10–25/IHD[b]	100%	Q24 hr
					<10/PD	100%	Q36 hr
Cefazolin **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function.	Renal (80%–100%)	1.5–2	Q8 hr	DI			
					11–30	25 mg/kg	Q12 hr
					≤10/IHD[b]/PD	25 mg/kg	Q24 hr

Continued

TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Cefdinir	Renal (10%–20%)	1–2	Q12–24 hr	D, I	<30	7 mg/kg (max 300 mg)	Q24 hr
					IHD[d]/PD	7 mg/kg (max 300 mg)	Q48 hr
Cefepime **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function.	Renal (85%)	2	Q8 hr	D, I	30-60	100%	Q12 hr
					10-29	100%	Q24 hr
					<10/PD/HD	50%	Q24 hr
Cefixime[c]	Renal (50%)/ (biliary)	3–4	Q12–24 hr	D	21–60/IHD	65%	Q12–24 hr
					<20/PD	45%	Q12–24 hr
Cefotaxime	Renal (60%)	1–1.5	Q6–8 hr	I	30–50	100%	Q8–12 hr
					10–29	100%	Q12 hr
					<10/IHD[b]/PD	100%	Q24 hr
Cefotetan	Renal (50%–80%) (biliary)	3–4.5	Q12 hr	D, I	10–30	50%	Q12 hr
					<10/IHD[d]/PD	50%	Q24 hr
Cefoxitin	Renal (85%)	0.75–1	Q4–8 hr	I	30–50	100%	Q8 hr
					10–30	100%	Q12 hr
					<10/IHD[b]/PD	100 %	Q24 hr
Cefpodoxime	Renal (30%)	2–3	Q12 hr	I	<30	100%	Q24 hr
					IHD	Administer thrice weekly after dialysis sessions	
Cefprozil	Renal (60%)	1.5	Q12–24 hr	D	<30/IHD[b]/PD	50%	Q12–24 hr

Ceftaroline[c]	Renal (88%)	1.5–2.5	Q8–12 hr	D, I	31–50	66%	Q8–12 hr
					15–30	50%	Q8–12 hr
					<15	33%	Q8–12 hr
					IHD[b]	33%	Q12 hr
Ceftazidime **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function.[3]	Renal (80%–90%)	1–2	Q8 hr	D, I	30–50	100%	Q12 hr
					10–30	100%	Q24 hr
					<10/IHD[b]/PD	50%	Q24 hr
Ceftibuten	Renal (60%)	2–2.5	Q24 hr	D	30–49	50%	Q24 hr
					5–29	25%	Q24 hr
					IHD	100%	After each dialysis session.
Cefuroxime (IV)	Renal (>90%)	1.5–2	Q8 hr	I	10–29	100%	Q12 hr
					<10/IHD[d]/PD	100%	Q24 hr
Cephalexin	Renal (>90%)	0.5–2.5	Q6–12 hr	I	30–50	100%	Q8 hr
					10–29	100%	Q12 hr
					<10/IHD[b]/PD	100%	Q24 hr
Ciprofloxacin	Renal (30%–50%) (hepatic)	3–5	Q8–12 hr	I	10–29	100%	Q18 hr
					<10/IHD[b]/PD	100%	Q24 hr

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Clarithromycin	Renal (20%–40%) (hepatic)	3–7	Q12 hr	D, I	<30 <10/IHD[b]/PD	50% 50%	Q12 hr Q24 hr
Ertapenem[c]	Renal (80%) (hepatic)	2.5–4	Q12–24 hr	D	≤30/IHD/PD	50%	Q12–24 hr
					IHD: If administered within 6 hr before dialysis, administer 30% of the daily dose as a supplemental dose after dialysis		
Erythromycin	Hepatic (renal [<15%])	1.5–2	Q6–12 hr	D	<10/IHD/PD	50%–75%	Q6–12 hr
Ethambutol[7]	Renal (50%) (hepatic)	2.5–3.5	Q24 hr	I	<30, IHD[b]	100%	3 times weekly
					PD	Data are not available. Begin with IHD dosing. Monitor closely and consider therapeutic drug monitoring[7]	

Famciclovir[c]	Renal (73%) (hepatic)	Penciclovir: 2–3	Q8 hr	D, I	**Herpes Zoster Treatment[c]**		
					40–59	500 mg	Q12 hr
					20–39	500 mg	Q24 hr
					<20	250 mg	Q24 hr
					IHD	250 mg	After each dialysis session
					Recurrent Genital Herpes Treatment—Single Day Regimen[c]		
					40–59	500 mg	Q12 hr ×1 day
					20–39	500 mg	Once
					<20	250 mg	Once
					IHD	250 mg	Once after dialysis
					Recurrent Genital Herpes Suppression[c]		
					20–39	125 mg	Q12 hr
					<20	125 mg	Q24 hr
					IHD	125 mg	After each dialysis session
					Recurrent Herpes Labialis—Single Dose Regimen[c]		
					40–59	750 mg	Once
					20–39	500 mg	Once
					<20	250 mg	Once
					IHD	250 mg	Once after dialysis
					Recurrent Orolabial or Genital Herpes in HIV-Infected Patients[c]		
					20–39	500 mg	Q24 hr
					<20	250 mg	Q24 hr
					IHD	250 mg	After each dialysis session

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Fluconazole	Renal (80%)	20–25	Q24 hr	D, I	10–50	50%	Q24 hr
					<10/PD	50%	Q48 hr
					IHD	100%	After each dialysis session
Flucytosine[8] **Note:** If available, therapeutic drug monitoring should be used to guide optimal dosing. Avoid flucytosine in children with severe kidney impairment.[9]	Renal (90%)	3–8	Q6 hr	I	20–40	100%	Q12 hr
					10–20	100%	Q24 hr
					<10/PD	100%	Q48 hr
					IHD	100%	After each dialysis session
Foscarnet	Renal (80%–90%)	Plasma: 3–4 Terminal: 88	Induction: Q8 h Maintenance: Q24 hr	D, I	See package insert for adjustments for induction and maintenance.[10]		
Ganciclovir	Renal (>80%)	2.5–3.5	Induction: Q12 hr Maintenance: Q24 hr	D, I	**Induction IV**		
					50–69	2.5 mg/kg	Q12 hr
					25–49	2.5 mg/kg	Q24 hr
					10–24	1.25 mg/kg	Q24 hr
					<10/PD/IHD[b]	1.25 mg/kg	Thrice weekly

					Maintenance IV		
					50–69	2.5 mg/kg	Q24 hr
					25–49	1.25 mg/kg	Q24 hr
					10–24	0.625 mg/kg	Q24 hr
					<10/PD/IHD[b]	0.625 mg/kg	Thrice weekly
Gentamicin	Renal (70%)	1.5–3	Q8–12 hr	I	<50/IHD/PD	Administer standard initial dose. Determine appropriate interval for redosing based on serum concentrations.	
Imipenem/cilastatin[c] **Note:** Patients with eGFR ≤15 should not receive imipenem/cilastatin unless dialysis will be initiated within 48 hr.[11]	Renal (70%)	1	Q6 hr	D, I	60-89	75%	Q8 hr
					30–59	50%	Q6 hr
					10–29	50%	Q12 hr
					<10/IHD[b]/PD	50%	Q24 hr
Isoniazid	Renal (75%–95%) (hepatic)	Slow acetylator: 2–5 Fast acetylator: 0.5–1.5	Q24 hr		IHD[b]	100%	Q24 hr
Lamivudine[12,c] **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function. If eGFR <5 or IHD, administer 50% of full dose as initial dose.	Renal	2	Q12 hr	D, I	30–49	100%	Q24 hr
					15–29	66%	Q24 hr
					5–14	33%	Q24 hr
					<5/IHD[b]/PD	17%	Q24 hr

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Levofloxacin	Renal (90%)	5–8	Q12	I	10–29	100%	Q24 hr
Note: Administer full dose for initial dose, then adjust subsequent doses for kidney function.					<10/IHD/PD	100%	Q48 hr
			Q24h	D, I	10–29	100%	Q48h
					<10/IHD/PD	67%	Q48h
Meropenem	Renal (70%)	1–1.5	Q8 hr	D, I	30–50	100%	Q12 hr
					10–29	50%	Q12 hr
					<10/IHD[b]/PD	50%	Q24 hr
Metronidazole	Hepatic [renal (15%)]	6–12	Q6–12 hr	D	<10	Renally eliminated metabolites may accumulate and lead to adverse events. Monitor patient. Some recommend a dose of 4 mg/kg at standard intervals.[1,2]	
					IHD[d]	4 mg/kg	Q6 hr
					PD	4 mg/kg	Q6 hr
Norfloxacin[c]	Hepatic (renal [30%])	3–4	Q12 hr	I	<30	100%	Q24 hr

Oseltamivir[c]	Oseltamivir carboxylate: Renal (>99%)	Oseltamivir carboxylate: 6–10	Q12–24 hr	D, I	**Influenza Treatment**		
					31–60	50%	Q12 hr
					11–30	50%	Q24 hr
					<10/IHD	25–40%	Once, then after each dialysis session
					PD	50%	Once
					Influenza Prophylaxis		
					31–60	50%	Q24 hr
					10–30	50%	Q48 hr
					<10	No recommended dosage regimen.	
					IHD	50%	Once, then after every other dialysis session
					PD	50%	Weekly for duration of prophylaxis

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Penicillin G—aqueous (K^+, Na^+) (IV) **Note:** Administer full dose for initial dose, then adjust subsequent doses for kidney function.	Renal (60%–85%) (hepatic)	0.5–1.2 hr	Q4–6 hr	D	10–50 <10/IHD[b]/PD	75% 50%	Q4–6 hr Q4–6 hr
Penicillin V K^+ (PO)	Renal (20-40%) (hepatic)	0.5 hr	Q6–8 hr	I	<10/IHD[b]/PD	100%	Q8 hr
Pentamidine[2]	Renal	5–9	Q24 hr	I	10–30 <10/IHD[b]/PD	100% 100%	Q36 hr Q48 hr
Piperacillin/tazobactam[1,2]	Renal (75%–90%/>80%)	0.7–1/0.7–1.5	Q6 hr	D, I	20–40 <20 IHD[b]/PD	70% 70% 70%	Q6 hr Q8 hr Q8–12 hr
Posaconazole	Fecal (Renal)	24–36	Oral suspension: Q8h Oral extended release, IV: Q12–24 hr	NA	<50	Consider risks and benefits of use of the IV product as solubilizing agent may accumulate. With PO products, exposure may vary, and breakthrough infections may occur.	

Rifabutin	Metabolites: Renal (50%) (hepatic)	35–45	Q24 hr	D	<30	50%-100%	Q24 hr
Streptomycin sulfate[c] **Note:** Determine appropriate interval for redosing based on serum concentration when available.	Renal (30%–90%)	2–5	Q24 hr	I	10–50 <10 IHD/PD	100% 100% 100%	Q24–72 hr Q48–96 hr. Administer 2–3 times weekly after dialysis
Sulfamethoxazole/trimethoprim	Renal (85%)/Renal (65%)	Sulfamethoxazole: 9–12 Trimethoprim: 3–8	Q8–12 hr	D	<30, IHD[b]/PD	50%	Q8–12 hr
Tetracycline[2,b]	Renal (30%–60%) (hepatic)	6–12	Q6 hr	I	50–80 10–50 <10	100% 100% 100%	Q8–12 hr Q12–24 hr Q24 hr
Tobramycin	Renal (>90%)	1.5–3	Q8–24 hr	I	<60	Administer standard initial dose. Determine appropriate interval for redosing based on serum concentrations.	

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Valacyclovir[c] **Note:** For IHD for all indications, dose for eGFR <10 and administer dose after dialysis. For PD for all indications, administer 500 mg Q48 hr.[4]	Hepatic to acyclovir.	Valacyclovir: ~30 min Acyclovir: 2–3	Q8–24 hr	D, I	**Herpes Zoster (Adults)**		
					30–49	100%	Q12 hr
					10–29	100%	Q24 hr
					<10	50%	Q24 hr
					Genital Herpes (Adolescents/Adults): Initial Episode		
					10–29	100%	Q24 hr
					<10	50%	Q24 hr
					Genital Herpes (Adolescents/Adults): Recurrent Episode		
					<30	100%	Q24 hr
					Genital Herpes (Adolescents/Adults): Suppressive		
					<30	500 mg	Q24 hr (for usual dose of 1 g Q24 hr)
						OR	
						500 mg	Q48 hr (for usual dose of 500 mg Q24 hr)
					Herpes Labialis (Adolescents/Adults)		
					30–49	50%	Q12 hr ×2 doses
					10–29	25%	Q12 hr ×2 doses
					<10	25%	Single dose

Valganciclovir **Note:** For dosing in children, a maximum eGFR value of 150 mL/min/1.73 m^2 should be used to calculate the dose. Calculate eGFR using modified Schwartz formula where k = 0.33 in infants aged <1 year, with low birth weight for gestational age, 0.45 in infants aged <1 year, with birth weight appropriate for gestational age, 0.45 in children aged 1 to <2 years, 0.55 in boys aged 2 to <13 years and girls aged 2 to <16 years, and 0.7 in boys aged 13–16 years. Consider use of k = 0.413 when enzymatic creatinine assays are used.	Ganciclovir: Renal (>80%)	Valganciclovir: 0.4–0.6 Ganciclovir: 2.5–3.5	Q12–24 hr	D, I	**Children**		
					Normal dosing accounts for kidney function:		
					Once daily dose (mg) = 7× body surface area × creatinine clearance.		
					Adults–Induction		
					40–59	450 mg	Q12 hr
					25–39	450 mg	Q24 hr
					10–24	450 mg	Q48 hr
					<10/IHD[b] (limited data-consider ganciclovir)	200 mg	Thrice weekly
					Adults–Maintenance		
					40–59	450 mg	Q24 hr
					25–39	450 mg	Q48 hr
					10–24	450 mg	Twice weekly
					<10/IHD[b] (limited data-consider ganciclovir)	200 mg	Thrice weekly

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TABLE 31.1

ANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics				Adjustments in Renal Failure		
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Vancomycin	Renal (80%–90%)	2.2–8	Q6–12 hr	I	<50	Administer standard initial dose. Determine appropriate interval for redosing based on serum concentrations.	
					IHD/PD	Administer standard initial dose. Obtain serum concentration after dialysis to determine need to redose. Obtain levels 4–6 hr after dialysis to allow for redistribution from peripheral compartment. If patient is unstable, may obtain sooner with knowledge that concentration may be lower than steady state.	

[a] Percentage in parenthesis represents the amount of drug and/or metabolites excreted in the urine. Route in parentheses indicates secondary route of excretion.

[b] For IHD administer after dialysis on dialysis days.

[c] In adults; guidelines not established in children.

[d] Administer a supplemental dose after dialysis

D, Dose reduction; *eGFR*, estimated glomerular filtration rate; *HIV*, human immunodeficiency virus; *hr*, hour; *I*, interval extension; *IHD*, intermittent hemodialysis; *IM*, intramuscular; *IV*, intravenous; K^+, potassium; *NA*, not applicable; Na^+, sodium; *PD*, peritoneal dialysis; *PO*, oral; *Q*, every; $t_{1/2}$, half-life with normal renal function.

III. NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE (Table 31.2)

TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE[1–5]

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Acetaminophen	Hepatic	2–4	Q4–6 hr	I	10–50 <10/IHD/PD	100% 100%	Q6 hr Q8 hr
Acetazolamide	Renal (>70%)	2.4–5.8	Q6–24 hr	I	10–50 IHD[b] <10/PD	100% 12.5%—titrate to effect Avoid use	Q12 hr Q12–24 hr
Allopurinol	Renal	1–3	Q6–24 hr	D	10–50 <10/IHD/PD	50% 30%	Q6–24 hr Q6–24 hr
Aminocaproic acid	Renal (76%)	1–2	Q4–6 hr, continuous	D	Oliguria/ESRD	12%–25%	Q4–6 hr, continuous
Aspirin	Hepatic (renal)	Dose dependent: 3–10	Q4–24 hr	I	10–50 IHD[b] <10/PD	100% 100% Avoid use for analgesia and antiinflammatory indications	Q4–24 hr Q24 hr
Atenolol	Renal (50%)	3.5–7	Q12–24 hr	D, I	15–35 <15/IHD[b]/PD	1 mg/kg up to 50 mg 1 mg/kg up to 25 mg	Q24 hr Q48 hr
Azathioprine	Hepatic to 6-mercaptopurine (renal)	2	Q24 hr	D	10–50 <10/IHD[b]/PD	75% 50%	Q24 hr Q24 hr

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TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Bismuth subsalicylate	Hepatic (renal)	Salicylate: 2–5 Bismuth: 21–72 days	Q3–4 hr		Avoid use in patients with renal failure.		
Bosentan	Hepatic (renal)	5	Q12 hr		Dose adjustment not required. Significant clearance by dialysis is not expected.		
Calcium supplements	GI (renal [20%])	Variable	Variable		<25	May require dosage adjustment depending on calcium level.	
Captopril	Renal (95%) (hepatic)	1.5–2	Q6–24 hr	D	10–50 <10/IHD[b]PD	75% 50%	Q6–24 hr Q6–24 hr
Carbamazepine **NOTE:** Avoid use of IV product in moderate to severe kidney dysfunction. Solubilizing agent may accumulate and lead to toxicity.	Hepatic (renal)	Initial: 25–65 Subsequent: 8–17	Q6–12 hr	D	<10/IHD[b]/PD	75%	Q6–12 hr
Cetirizine[2]	Renal (70%) (hepatic)	6–8	Q12–24 hr	D	10-29/IHD/PD ≤10	50% Use not recommended.	Q24 hr
Chloroquine	Renal (70%) (hepatic)	3–5 days	Weekly	D	<10/IHD/PD	50%	Weekly
Chlorothiazide	Renal (>90%)	0.75–2	Q12–24 hr	NA	<30 <10	May be ineffective. Use not recommended.	

Cimetidine	Renal (50%) (hepatic)	1.5–2	Q6–12 hr	D, I	10–50	50%	Q6–12 hr
					<10/IHD[b]/PD	100%	Q8–12 hr
Clobazam	Renal (82%) (Hepatic, GI)	Children: 16 Adults: 36–42	Q12–24 hr	D	<30	Use with caution; has not been studied.	
Desloratadine[c]	Renal (87%) (GI)	27	Q24 hr	I	<50	100%	Q48 hr
Digoxin	Renal (50%–70%) (GI)	18–48		D, I			
					Digitalizing Dose		
					ESRD	50%	NA
					Maintenance Dose		
					30–50	75%	Q12–24 hr
					10–29	50%	Q12–24 hr
						OR 100%	Q36 hr
					<10/IHD/PD	25%	Q12–24 hr
						OR 100%	Q48 hr
Disopyramide[c]	Renal (40%–60%) (GI)	3–10	Q6 hr	I	30–40	100%	Q8 hr
					15–30	100%	Q12 hr
					<15	100%	Q24 hr

Continued

TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
EDTA calcium disodium[c] **Note:** Do not administer in patients with anuria or severe oliguria.	Renal	1.5 (IM) 0.3–1 (IV)	IM: Q8–12 hr IV: Q24 hr	D, I	**IV: Adult Serum Creatinine-Based Dosing**		
					≤2 mg/dL	1 g/m^2	Q24 hr ×5 days
					2–3 mg/dL	500 mg/m^2	Q24 hr ×5 days
					3–4 mg/dL	500 mg/m^2	Q48 hr ×3 doses
					>4 mg/dL	500 mg/m^2	Once weekly
Enalapril (IV: enalaprilat)	Renal (60%–80%) (hepatic)	1.5–6 (PO) 5–20 (IV)	Q6–24 hr	D	10–50	75%	Q6–24 hr
					<10	50%	Q6–24 hr
					Manufacturer does not recommend in infants and children aged ≤16 years with GFR <30 mL/min/1.73 m^2.		
Enoxaparin[c]	Renal (40%)	4.5–7	Q12–24 hr	I	<30	100%	Q24 hr
					IHD/PD	Serious bleeding complications may occur in this population. Avoid use. If used, reduce dose and monitor anti-Xa activity.[5]	
Epoprostenol	Hydrolyzed to renally eliminated metabolites (85%)	6 min	Continuous infusion	D	Manufacturer does not recommend renal dose reduction. Titrate to clinical effect.		
Famotidine	Renal (70%)	2–3	Q12–24 hr	D, I	30–50	100%	Q24 hr
					10–29	50%	Q24 hr
					<10/IHD/PD	25%	Q24 hr

Felbamate[c]	Renal (50%)	20–30	Q6–8 hr	D	<50	50%	Q6–8 hr
Fentanyl	Hepatic (renal [75%])	Single dose: 2–4 Prolonged infusion: 21	Q30 min–1 hr, continuous Patch: Q72 hr	D	**Injection**		
					<50	Manufacturer does not recommend dose reduction. Titrate to clinical effect.	
					Patch		
					Mild–moderate impairment	Initial dose: 50%	Q72 hr
					Severe impairment	Not recommended.	
Fexofenadine	GI (renal [12%])	14	Q12 hr	I	<50	100%	Q24 hr
Flecainide[c]	Hepatic (Renal [>80%])	8–20	Q8–12 hr	D	<35	50%	Q12 hr
Furosemide	Renal (50%–80%) (hepatic)	0.5	PO: Q6–24 hr IV: Q6–12 hr		Avoid use in oliguria.		
Gabapentin	Renal (>75%) (GI)	5	Q8 hr	D, I	30–59	75%	Q12 hr
					15–29	75%	Q24 hr
					<15/IHD[d]/PD	75%	Q48 hr
Hydralazine[e]	Hepatic (renal [14%])	2–8	IV: Q4–6 hr PO: Q6–12 hr	I	10–50	100%	Q8 hr (fast acetylator)
					<10/IHD/PD	100%	Q8–16 hr Q12–24 hr (slow acetylator)
Iloprost[c]	Renal (70%) [Hepatic]	20–30 min	Q2–4 hr inhalation, continuous inhalation	D, I	<10/IHD/PD	Use with caution; has not been studied.	
Insulin (regular)[f]	Hepatic (renal)	IV: 0.5–1 Subcutaneous: 1.5	Variable	D	10–50	75%	No change
					<10/IHD/PD	50%	No change

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TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Ivacaftor	Hepatic (>85%)	12	Q12 hr	NA	<30	Use with caution.	
Lacosamide[c]	Renal (95%) (GI)	13	Q12 hr	D	<30	Maximum dose: 300 mg/24-hr period	
					IHD	Administer 50% dose supplementation after 4-hr dialysis session.	
Levetiracetam	Renal (66%)	5–8	Q12 hr	D, I	**Children**		
					<50	50%	Q12 hr
					IHD[g]/PD	50%	Q24 hr
					Adults		
					50–80	500–1000 mg	Q12 hr
					30–50	250–750 mg	Q12 hr
					<30	250–500 mg	Q12 hr
					IHD[g]/PD	500–1000 mg	Q24 hr
Lisinopril	Renal	11–13	Q24 hr	D	10–50	50%	Q24 hr
					<10/IHD[b]/PD	25%	Q24 hr
					Per manufacturer, use not recommended for children with eGFR <30 mL/min/1.73 m^2.		
Lithium[1] **Note:** Monitor serum concentrations. Due to high volume of distribution, lithium concentrations rebound after dialysis.[2]	Renal (>90%)	18–36	Q8–12 hr	D	10–50	50–75%	Q8–12 hr
					<10	25–50%	Q8–12 hr
					IHD	Dose after dialysis. Doses may vary, use serum concentrations to guide.	

Loratadine	Hepatic (renal 40%])	Loratadine: 8.4 Metabolite: 28	Q24 hr	I	<10/IHD	100%	Q48 hr
Lumacaftor + Ivacaftor	Hepatic (renal)	Lumacaftor: 26 Ivacaftor: 9	Q12 hr	NA	<30	Use with caution.	
Meperidine **Note:** Accumulation of normeperidine can lead to tremors and seizures. Limit duration to ≤48 hr in all patients. Avoid use in patients with kidney dysfunction.[1]	Renal (hepatic) (normeperidine, renal)	Meperidine: 2.3–4 Normeperidine: 8-20	Q3–4 hr	D	10–50	75%	Avoid use, especially repeat administrations.
					<10	50%	Avoid use, especially repeat administrations.
					IHD/PD	Avoid use.	
Methadone	Hepatic (renal [<10%])	20–35	Q6–12 hr	D	<10/IHD/PD	50%–75%	Q6–12 hr
Methyldopa	Hepatic (renal [70%])	1–3	PO: Q6–12 hr IV: Q6–8 hr	I	>50	100%	Q8 hr
					10–50	100%	Q8–12 hr
					<10/IHD[b]/PD	100%	Q12–24 hr
Metoclopramide	Renal (85%)	2.5–6	PO: Q6 hr IV: Q6–8 hr	D	30–50	75%	No change
					10–30	50%	No change
					<10/IHD/PD	25%	No change

Continued

TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion**[a]	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Midazolam **Note:** Metabolite α-hydroxymidazolam can accumulate in kidney failure, leading to prolonged sedation after midazolam is discontinued.[4]	Hepatic (renal [>60% as α-hydroxymidazolam])	2.5–4.5	Variable	D	<10	50%	No change
Milrinone	Renal (>85%)	1.5–2.5	Continuous infusion	D	50 40 30 20 10 5		0.43 mCg/kg/min 0.38 mCg/kg/min 0.33 mCg/kg/min 0.28 mCg/kg/min 0.23 mCg/kg/min 0.2 mCg/kg/min
Morphine	Hepatic (renal [5%–15%])	1–8	Variable	D	10–50 <10/IHD/PD	75% 50%	No change No change
Neostigmine	Hepatic (renal [50%])	0.5–2	Variable	D	10–50 <10	50% 25%	No change No change
Oxcarbazepine	Hepatic (Renal)	Oxcarbazepine: 2 MHD metabolite: 9	Q12 hr	D	<30	Initial dose: 50%. Titrate slowly.	Q12 hr
Pancuronium bromide	Renal (40%) (hepatic)	1.5–2.5	Q30–60 min *OR* continuous infusion	D	10–50 <10/IHD/PD	50% Avoid use.	No change

Phenazopyridine	Renal (65%) (hepatic)	Unavailable	Q8 hr for 2 days	I	50–80 <50	100% Contraindicated	Q8–16 hr
Phenobarbital	Hepatic (renal [20%–50%])	35–140	Q8–12 hr	I	<10/IHD[b]	100%	Q24 hr
Primidone **Note:** Due to complex metabolism, it is preferred to use other options when available for patients with kidney failure.[5]	Hepatic (renal [20%])	Primidone: 10–12 PEMA metabolite: 16 Phenobarbital: 35–140	Q6–12 hr	I	>50 10–50 <10/IHD[b]	100% 100% 100%	Q12 hr Q12–24 hr Q24 hr
Procainamide	Hepatic (renal [Procainamide 50%, NAPA 80%])	Procainamide: 1.7–4. 7 NAPA: 6	PO: Q4–6 hr IV: continuous	D	**IV Loading Dose**		
					<10	12 mg/kg	Once
					IV Maintenance[c]		
					<10	Initiate at low end of dosing range and titrate to effect.	
					IHD	Monitor levels. Supplementation may be needed.	
Quinidine	Renal (15%–25%)	2.5–8	Q6–12 hr	D	<10/IHD[b]/PD	75%	Q6–12 hr
Ranitidine	Renal (30%–70%) (hepatic)	1.5–2.5	PO: Q12 hr IV/IM: Q6–8 hr	D, I	30–50 10–29 <10/IHD[b]/PD	100% 50% 50%	Q12 hr Q12 hr Q24 hr
Sodium phenylacetate and sodium benzoate	Renal	Unavailable	Continuous	D	<50	Use with caution and close monitoring.	

Continued

TABLE 31.2

NONANTIMICROBIALS REQUIRING ADJUSTMENT IN RENAL FAILURE—cont'd

	Pharmacokinetics			Adjustments in Renal Failure			
Drug	**Route of Excretion[a]**	**Normal $t_{1/2}$ (hr)**	**Normal Dose Interval**	**Method**	**eGFR (mL/min/1.73 m^2)**	**Percentage of Usual Dose**	**Interval**
Spironolactone	Renal (hepatic/biliary)	Spironolactone: 1.3–1.4 Metabolite: 13–24	Q6–24 hr	I	30–50 <30	100% Avoid use.	Q24 hr
Terbutaline	Renal (60%) (hepatic)	2.9–14	PO: Q8 hr Subcutaneous: Q2–6 hr IV: Continuous	D	<50	Manufacturer does not recommend dose reduction. Use with caution.	
Tezacaftor + Ivacaftor	Hepatic (renal)	Tezacaftor: 15 Ivacaftor:13	Combo product in AM, ivacaftor 12 hr after	NA	<30	Use with caution.	
Treprostinil	Renal (80%)	4	Oral: Q8–12 hr SubQ/IV: continuous	D, I	Manufacturer does not recommend dose reduction. Use with caution.		
Triamterene	Hepatic (renal [21%])	1.6–2.5	Q12–24 hr	I	<30	Do not use due to risk of hyperkalemia.[1]	
Verapamil	Renal (70%) (hepatic)	2–8	Variable	D	<10	Dose reduction may be needed; use caution. Monitor blood pressure, ECG for PR prolongation, and other signs of overdose.	

Vigabatrin	Renal (80%)	5–10	Q12 hr	D	50–80	75%	Q12 hr
					30–50	50%	Q12 hr
					10–30	25%	Q12 hr

[a] Percentage in parentheses represents the amount of drug and/or metabolites excreted in the urine. Route in parentheses indicates secondary route of excretion.

[b] For IHD administer after dialysis on dialysis days.

[c] In adults; guidelines not established in children.

[d] Administer supplemental dose after every 4 hours of dialysis, based on daily dose as follows (daily dose/recommended supplemental dose): 100 mg/125 mg; 125 mg/150 mg; 150 mg/200 mg; 200 mg/250 mg; 300 mg/350 mg.

[e] Dose interval varies for rapid and slow acetylators with normal and impaired renal function.

[f] Renal failure may cause hyposensitivity or hypersensitivity to insulin. Empiric dosing recommendations may not be appropriate for all patients; adjust to clinical response and blood glucose.

[g] Administer a supplemental dose after dialysis.

D, Dose reduction; *ECG*, electrocardiogram; *EDTA*, ethylenediaminetetraacetic acid; *eGFR*, estimated glomerular filtration rate; *ESRD*, end-stage renal disease; *GI*, gastrointestinal; *I*, interval extension; *IHD*, hemodialysis; *IM*, intramuscular; *IV*, intravenous; *MHD*, 10-monohydroxy metabolite; *NA*, not applicable; NAPA, *N*-acetylprocainamide; *PD*, peritoneal dialysis; *PO*, oral; *Q*, every; *SubQ*, subcutaneous; $t_{1/2}$, half-life.

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